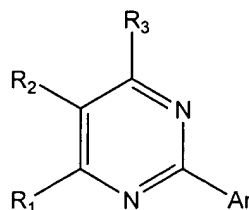


WHAT IS CLAIMED IS:

1. A compound of the formula:



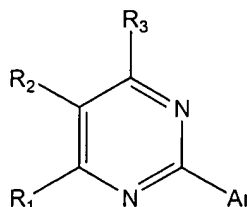
5 or a pharmaceutically acceptable salt thereof, wherein:

Ar is phenyl, 1- or 2-naphthyl, each of which is mono-, di-, or tri-substituted or mono-, di-, or tri-substituted heteroaryl having from about 5 to about 7 ring members and 1 to about 4 heteroatoms in the ring, the heteroatoms independently selected from the group consisting of N, O and S;

10 R₁ and R₃ are independently chosen from hydrogen, halogen, cyano, nitro, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted (cycloalkyl)alkyl, optionally substituted alkylthio, optionally substituted alkylsulfinyl, optionally substituted alkylsulfonyl, or optionally substituted mono- or dialkylcarboxamide, with the
15 proviso that R₁ and R₃ are not both hydrogen; and

R₂ is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted aminoalkyl, optionally substituted mono or dialkylamino, optionally substituted alkylthio, optionally substituted alkylsulfinyl, optionally substituted alkylsulfonyl, optionally substituted
20 mono or dialkylcarboxamide, optionally substituted carbocyclic aryl or optionally substituted heteroaryl having from 1 to 3 rings, and 3 to 8 ring members in each ring and 1 to about 3 heteroatoms..

2. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

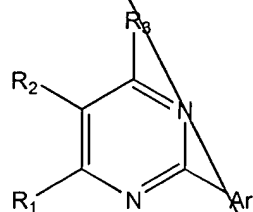
Ar is phenyl which is mono-, di-, or tri-substituted;

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*cont*⁵
R₁ and R₃ are independently chosen from hydrogen, halogen, cyano, nitro, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted (cycloalkyl)alkyl, optionally substituted alkylthio, optionally substituted alkylsulfinyl, or optionally substituted alkylsulfonyl, and optionally substituted mono or dialkylcarboxamide, with the proviso that R₁ and R₃ are not both hydrogen; and

10 R₂ is optionally substituted alkyl, optionally substituted alkoxy, optionally substituted aminoalkyl, optionally substituted mono or dialkylamino, optionally substituted alkylthio, optionally substituted alkylsulfinyl, optionally substituted alkylsulfonyl, optionally substituted mono or dialkylcarboxamide, or

15 R₂ is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, pyridizynyl, and thiophenyl, each of which is optionally mono-, di-, or tri-substituted.

3. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein:

20 R₁ and R₃ are independently selected from hydrogen, halogen, cyano, C₁₋₆ alkyl₁, (C₃₋₇cycloalkyl₁)C₁₋₄alkyl₁, -O(C₃₋₇cycloalkyl₁)C₁₋₄alkyl₁, halo(C₁₋₆)alkyl₁, -O(halo(C₁₋₆)alkyl₁), -O(C₁₋₆alkyl₁), and S(O)_n(C₁₋₆alkyl₁),

25 where each alkyl₁ is independently straight, branched, or cyclic, may contain 1 or more double or triple bonds, and is optionally substituted with one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C₁₋₄alkoxy, amino, and mono- or di(C₁₋₄)alkylamino, and

where each C₃₋₇cycloalkyl₁ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C₁₋₄alkoxy, amino, and mono- or di(C₁₋₄)alkylamino,

with the proviso that not both R₁ and R₃ are hydrogen;

R₂ is selected from the group consisting of -XR_A and Y; and

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, pyridiziny, and thiophenyl, each of which is mono-, di-, or tri-substituted with R_C;

R_A and R_B, which may be the same or different, are independently selected at each occurrence from:

hydrogen and straight, branched, or cyclic alkyl groups, including (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, which straight, branched, or cyclic alkyl groups may contain one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, cyano, amino, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), -NHC(=O)(C₁₋₆alkyl), -N(C₁₋₆alkyl)C(=O)(C₁₋₆alkyl), -NHS(O)_n(C₁₋₆alkyl), -S(O)_n(C₁₋₆alkyl), -S(O)_nNH(C₁₋₆alkyl), -S(O)_nN(C₁₋₆alkyl)(C₁₋₆alkyl), and Z;

R_C is independently selected at each occurrence from halogen, cyano, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R_D, C₂₋₆alkenyl substituted with 0-2 R_D, C₂₋₆alkynyl substituted with 0-2 R_D, C₃₋₇cycloalkyl substituted with 0-2 R_D, (C₃₋₇cycloalkyl)C₁₋₄alkyl substituted with 0-2 R_D, C₁₋₆alkoxy substituted with 0-2 R_D, -NH(C₁₋₆alkyl) substituted with 0-2 R_D, -N(C₁₋₆alkyl)(C₁₋₆alkyl) each C₁₋₆alkyl independently substituted with 0-2 R_D, -XR_A, and Y;

R_D is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, amino, C₁₋₄alkyl, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), -S(O)_n(alkyl), halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋₄alkyl), CONH(C₁₋₄alkyl), CON(C₁₋₄alkyl)(C₁₋₄alkyl), -XR_A, and Y;

B1 cont

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR_B-, -O-, -C(=O)-, -C(=O)O-, -S(O)_n-, -NH-, -NR_B-, -C(=O)NH-, -C(=O)NR_B-, -S(O)_nNH-, -S(O)_nNR_B-, -OC(=S)S-, -NHC(=O)-, -NR_BC(=O)-, -NHS(O)_n-, -OSiH_n(C₁₋₄alkyl)_{2-n}-, and -NR_BS(O)_n-;

5 Y and Z are independently selected at each occurrence from: 3- to 7-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, cyano, C₁₋₄alkyl, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), and -S(O)_n(alkyl),

10 said 3- to 7-membered heterocyclic groups containing one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen; and

n is independently selected at each occurrence from 0, 1, and 2.

Sub E

15 4. A compound or salt according to Claim 1 wherein Ar is mono-, di-, or trisubstituted phenyl; and R₂ is selected from optionally substituted alkoxy, optionally substituted aminoalkyl, and optionally substituted mono or dialkylamino.

20 5. A compound or salt according to Claim 3, wherein: Ar is phenyl mono-, di-, or tri-substituted with R_C.

25 6. A compound or salt according to Claim 3, wherein: Ar is phenyl mono-, di-, or tri-substituted with R_C; and R₁ and R₃ are independently selected from the group consisting of halogen, C₁₋₃alkyl, C₁₋₃alkoxy, (C₃₋₇cycloalkyl)C₁₋₃alkyl, (C₃₋₇cycloalkyl) C₁₋₃alkoxy, each of which is unsubstituted or substituted by 1-3 groups independently chosen from hydroxy, amino, cyano, and halogen.

sub B2

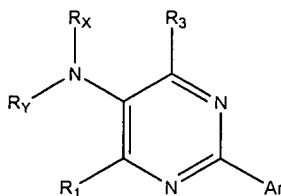
30 7. A compound or salt according to Claim 3, wherein:

B2
cont⁵

Ar is phenyl mono-, di-, or tri-substituted with R_C; and
R_A and R_B, which may be the same or different, are independently selected at each occurrence from:
straight, branched, or cyclic alkyl groups having from 1 to 8 carbon atoms, which alkyl groups may contain one or more double or triple bonds.

8. A compound or salt according to Claim 3, wherein:
Ar is phenyl mono-, di-, or tri-substituted with R_C;
R_A and R_B, which may be the same or different, are independently selected at each occurrence from:
straight, branched, or cyclic alkyl groups having from 1 to 8 carbon atoms, which alkyl groups may contain one or more double or triple bonds; and
R₁ and R₃ are independently selected from the group consisting of halogen,
C₁₋₃alkyl, C₁₋₃alkoxy, (C₃₋₇cycloalkyl)C₁₋₃alkyl, (C₃₋₇cycloalkyl) C₁₋₃alkoxy, each of which is unsubstituted or substituted by 1-3 groups independently chosen from hydroxy, amino, cyano, and halogen.

9. A compound of Formula A



Formula A

or a pharmaceutically acceptable salt thereof, wherein:

R_X and R_Y are the same or different and are independently selected from:

- a) hydrogen,
- b) -(C=O)alkyl_A, wherein alkyl_A is a straight or branched alkyl group having from 1 to 8 carbon atoms;
- c) straight, branched, or cyclic alkyl groups, including cycloalkyl(alkyl)groups, said alkyl groups having from 1 to 8 carbon

B²
atoms and optionally containing one or more double or triple bonds, each of which alkyl groups may be further substituted with one or more substituent(s) independently selected from:

- 5
- i) hydroxy, halogen, amino, cyano, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), and -NH(C₁₋₄alkyl)(C₁₋₄alkyl), and
- 10 ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents independently selected from halogen, halo(C₁₋₄alkyl), halo(C₁₋₄alkoxy), oxo, hydroxy, amino, C₁₋₄alkyl, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), and -S(O)_n(alkyl), wherein said 3- to 7-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen,
- 15

R₁ and R₃ are independently selected from hydrogen, halogen, cyano, C₁₋₆ alkyl₁, (C₃₋₇cycloalkyl₁)C₁₋₄alkyl₁, -O(C₃₋₇cycloalkyl₁)C₁₋₄alkyl₁, halo(C₁₋₆alkyl₁), -O(halo(C₁₋₆alkyl₁)), -O(C₁₋₆alkyl₁), and S(O)_n(C₁₋₆alkyl₁),

where each said alkyl₁ is straight, branched, or cyclic and may contain 1 or more double or triple bonds, and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C₁₋₄alkoxy, amino, and mono- or di(C₁₋₄)alkylamino, and

20

where said C₃₋₇cycloalkyl₁ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C₁₋₄alkoxy, amino, and mono- or di(C₁₋₄)alkylamino

25

with the proviso that not both R₁ and R₃ are hydrogen;

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with R_C;

30 R_A and R_B, which may be the same or different, are independently selected at each occurrence from the group consisting of:

B²
cont₅

hydrogen and straight, branched, or cyclic alkyl groups, including

(cycloalkyl)alkyl groups, consisting of 1 to 8 carbon atoms, which may contain one or more double or triple bonds, each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), -NHC(=O)(C₁₋₆alkyl), -N(C₁₋₆alkyl)C(=O)(C₁₋₆alkyl), -NHS(O)_n(C₁₋₆alkyl), -S(O)_n(C₁₋₆alkyl), -S(O)_nNH(C₁₋₆alkyl), -S(O)_nN(C₁₋₆alkyl)(C₁₋₆alkyl), and Z;

10 R_C is independently selected at each occurrence from halogen, cyano, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, and C₁₋₆alkyl substituted with 0-2 R_D, C₂₋₆ alkenyl substituted with 0-2 R_D, C₂₋₆alkynyl substituted with 0-2 R_D, C₃₋₇cycloalkyl substituted with 0-2 R_D, (C₃₋₇cycloalkyl)C₁₋₄alkyl substituted with 0-2 R_D, C₁₋₆alkoxy substituted with 0-2 R_D, -NH(C₁₋₆alkyl) substituted with 0-2 R_D, -N(C₁₋₆alkyl)(C₁₋₆alkyl) each C₁₋₄alkyl independently substituted with 0-2 R_D, -XR_A, and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimidine ring shown in Formula A is substituted;

15 R_D is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, C₁₋₄alkyl, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), -S(O)_n(alkyl) halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋₄alkyl), CONH(C₁₋₄alkyl), 20 CON(C₁₋₄alkyl)(C₁₋₄alkyl), -XR_A, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR_B-, -O-, -C(=O)-, -C(=O)O-, -S(O)_n-, -NH-, -NR_B-, -C(=O)NH-, -C(=O)NR_B-, -S(O)_nNH-, -S(O)_nNR_B-, -OC(=S)S-, -NHC(=O)-, -NR_BC(=O)-, -NHS(O)_n-, -OSiH_n(C₁₋₄-alkyl_{2-n})-, and -NR_BS(O)_n-;

25 Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C₁₋₄alkyl, -O(C₁₋₄alkyl), 30 -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), and -S(O)_n(alkyl); and

n is 0, 1, or 2.

10. A compound or salt according to Claim 9, wherein:

R_X and R_Y are the same or different and are independently selected from:

a) $-(C=O)alkyl_A$, wherein $alkyl_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

b) straight, branched, or cyclic alkyl groups, including cycloalkyl(alkyl)groups, said alkyl groups having from 1 to 8 carbon atoms and optionally containing one or more double or triple bonds, each of which alkyl groups may be further substituted with one or more substituent(s) independently selected from:

i) hydroxy, halogen, amino, cyano, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, and $-NH(C_{1-4}alkyl)(C_{1-4}alkyl)$, and

ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents independently selected from halogen, $halo(C_{1-4}alkyl)$, $halo(C_{1-4}alkoxy)$, oxo, hydroxy, amino, $C_{1-4}alkyl$, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$, and $-S(O)_n(alkyl)$, wherein said 3- to 7-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen,

R_1 and R_3 are independently selected from $C_{1-6}alkyl_1$, $(C_{3-7}cycloalkyl_1)C_{1-4}alkyl_1$, $-O(C_{3-7}cycloalkyl_1)C_{1-4}alkyl_1$, $halo(C_{1-6}alkyl_1)$, $-O(halo(C_{1-6}alkyl_1))$, and $-O(C_{1-6}alkyl_1)$, where each said $alkyl_1$ is straight, branched, or cyclic and may contain 1 or more double or triple bonds, and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, $C_{1-4}alkoxy$, amino, and mono- or di($C_{1-4}alkylamino$),

and

where said $C_{3-7}cycloalkyl_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, $C_{1-4}alkoxy$, amino, and mono- or di($C_{1-4}alkylamino$)

Ar is phenyl, which is mono-, di-, or tri-substituted with R_C ;

B1 cont
5 R_A and R_B , which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen and straight, branched, or cyclic alkyl groups, including (cycloalkyl)alkyl groups, consisting of 1 to 8 carbon atoms, which may contain one or more double or triple bonds, each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, C_{1-6} alkoxy, $-NH(C_{1-6}alkyl)$, $-N(C_{1-6}alkyl)(C_{1-6}alkyl)$, $-NHC(=O)(C_{1-6}alkyl)$, $-N(C_{1-6}alkyl)C(=O)(C_{1-6}alkyl)$, and Z;

10 R_C is independently selected at each occurrence from halogen, cyano, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, and C_{1-6} alkyl substituted with 0-2 R_D , C_{2-6} alkenyl substituted with 0-2 R_D , C_{2-6} alkynyl substituted with 0-2 R_D , C_{3-7} cycloalkyl substituted with 0-2 R_D , $(C_{3-7}cycloalkyl)C_{1-4}alkyl$ substituted with 0-2 R_D , C_{1-6} alkoxy substituted with 0-2 R_D , $-NH(C_{1-6}alkyl)$ substituted with 0-2 R_D , $-N(C_{1-6}alkyl)(C_{1-6}alkyl)$ each $C_{1-6}alkyl$ independently substituted with 0-2 R_D , -
15 XR_A , and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimidine ring shown in Formula A is substituted;

R_D is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, $C_{1-4}alkyl$, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$,
20 halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, $CO(C_{1-4}alkyl)$, $CONH(C_{1-4}alkyl)$, $CON(C_{1-4}alkyl)(C_{1-4}alkyl)$, $-XR_A$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_B-$, $-O-$, $-C(=O)-$, $-C(=O)O-$, $-NH-$, $-NR_B-$, $-C(=O)NH-$, $-C(=O)NR_B-$, $-NHC(=O)-$, and $-NR_BC(=O)-$;

25 Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, $C_{1-4}alkyl$, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, and $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$; and

30 n is 0, 1, or 2.

11. A compound or salt according to claim 9, wherein:

Ar is phenyl mono-, di-, or tri-substituted with R_C , and

R_1 and R_3 are independently selected from the group consisting of

hydrogen, halogen, C_{1-4} alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy,

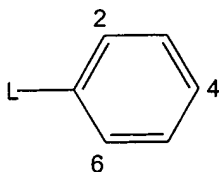
C_{1-6} alkyl, which C_{1-6} alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, C_{1-4} alkoxy, amino, and mono- or di(C_{1-4})alkylamino, and

(C_{3-7} cycloalkyl) C_{1-4} alkyl, which (C_{3-7} cycloalkyl) C_{1-4} alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, C_{1-4} alkoxy, amino, and mono- or di(C_{1-4})alkylamino.

10

12. A compound or salt according to claim 9, wherein:

Ar is a phenyl group of the formula:



15

wherein L indicates a bond to the pyrimidine ring in Formula A and the phenyl group is substituted at one, two, or three of positions 2, 4, and 6 positions of the phenyl ring with substituents independently selected from:

i) halogen, cyano, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, hydroxy, amino, C_{1-6} alkyl, C_{1-6} alkoxy, (C_{1-4} alkoxy) C_{1-4} alkoxy, and mono- or di(C_{1-4} alkyl)amino,

ii) C_{1-6} alkyl and C_{1-6} alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C_{1-4} alkyl, $-O(C_{1-4}$ alkyl), $-NH(C_{1-4}$ alkyl), and $-N(C_{1-4}$ alkyl)(C_{1-4} alkyl).

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13. A compound or salt according to claim 9, wherein:

Ar is phenyl mono-, di-, or tri-substituted with R_C ,

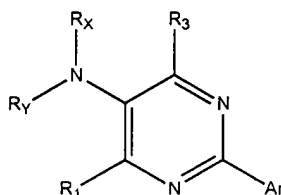
R_X and R_Y , which may be the same or different, are independently

selected at each occurrence from

straight, branched, or cyclic alkyl groups, including (cycloalkyl)alkyl groups, consisting of 1 to 8 carbon atoms, which may contain one or more double or triple bonds; and

- 5 R₁ and R₃ are independently selected from the group consisting of hydrogen, halogen, C₁₋₄alkoxy, halo(C₁₋₄)alkyl, (halo(C₁₋₄)alkoxy, C₁₋₆alkyl, which C₁₋₆alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, C₁₋₄alkoxy, amino, and mono- or di(C₁₋₄)alkylamino,
- 10 (C₃₋₇cycloalkyl)C₁₋₄alkyl, which (C₃₋₇cycloalkyl)C₁₋₄alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, C₁₋₄alkoxy, amino, and mono- or di(C₁₋₄)alkylamino.

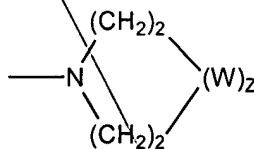
14. A compound or salt according to claim 3 of the formula:



R_X and R_Y are the same or different and are independently selected from the group consisting of:

hydrogen and C₁ – C₆ alkyl; or

NR_XR_Y represents:

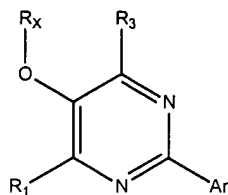


wherein:

z is 0 or 1; and

W is chosen from the group consisting of CR_AR_B, NR_B, and O.

15. A compound or salt according to claim 3, of the formula



5 wherein:

R_X is chosen from

straight, branched, or cyclic alkyl groups, including cycloalkyl(alkyl) groups, having from 1 to 8 carbon atoms, which may contain one or more double or triple bonds, each of which may be further substituted with one or more substituent(s) independently selected from:

(a) hydroxy, halogen, amino, cyano, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, and $-NH(C_{1-4}alkyl)(C_{1-4}alkyl)$, and

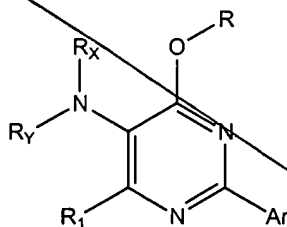
(b) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents selected from halogen, halo(C_{1-4})alkyl, oxo, hydroxy, amino, $C_{1-4}alkyl$, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$, wherein said 3- to 7-membered heterocyclic groups contain one or more heteroatom(s) selected from N, O, and S, with the point of attachment being either carbon or nitrogen.

20

16. A compound or salt according to claim 15 wherein:

R_1 and R_3 are independently selected from the group consisting of hydrogen, halogen, $C_{1-4}alkyl$, $C_{1-4}alkoxy$, and halo(C_{1-4})alkyl.

17. A compound or salt according to Claim 3 of Formula B:



Formula B

Ar is phenyl mono-, di-, or tri-substituted with R_C;

R is selected from straight, branched, or cyclic alkyl groups, including (cycloalkyl)alkyl groups, which may contain 1 or more double or triple bonds, and which are optionally substituted by one or more substituents independently chosen from oxo, hydroxy, halogen, cyano, -O(C₁₋₄ alkyl), amino, -NH(C₁₋₄ alkyl), and -N(C₁₋₄ alkyl)(C₁₋₄ alkyl);

R₁ is selected from hydrogen, halogen, cyano, C₁₋₄ alkyl, (C₃₋₇cycloalkyl)C₁₋₄alkyl, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, and -O(C₁₋₄alkyl); and

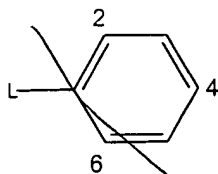
10 R_X and R_Y are the same or different and are independently selected from:

a) hydrogen,

b) -(C=O)alkyl_A, wherein alkyl_A is a straight or branched alkyl group having from 1 to 8 carbon atoms;

15 c) straight, branched, or cyclic alkyl groups, including cycloalkyl(alkyl) groups, having from 1 to 8 carbon atoms, which may contain one or more double or triple bonds, each of which may be further substituted with one or more substituent(s) independently selected from (i) hydroxy, halogen, amino, cyano, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), and -NH(C₁₋₄alkyl)(C₁₋₄alkyl), and
20 (ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents selected from halogen, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, oxo, hydroxy, amino, C₁₋₄alkyl, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), and -S(O)_n(alkyl), wherein said 3- to 7-membered heterocyclic groups contain one or more heteroatom(s)
25 independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen.

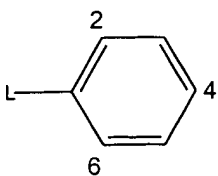
18. A compound or salt according to Claim 17, wherein Ar is a phenyl group of the formula:



wherein L indicates a bond to the pyrimidine ring in Formula B and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituents independently selected from:

- 5 i) halogen, cyano, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, hydroxy, amino, C₁₋₆ alkyl, C₁₋₆alkoxy, (C₁₋₄alkoxy)C₁₋₄alkoxy, and mono- or di(C₁₋₄alkyl)amino,
- ii) C₁₋₆ alkyl and C₁₋₆alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further
- 10 substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C₁₋₄alkyl, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), and -N(C₁₋₄alkyl)(C₁₋₄alkyl).

19. A compound or salt according to Claim 17, wherein Ar is a phenyl group of the formula:



wherein L indicates a bond to the pyrimidine ring in Formula B and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituents independently selected from:

- 20 i) halogen, cyano, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, hydroxy, amino, C₁₋₆ alkyl, C₁₋₆alkoxy, (C₁₋₄alkoxy)C₁₋₄alkoxy, and mono- or di(C₁₋₄alkyl)amino,
- ii) C₁₋₆ alkyl and C₁₋₆alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further
- 25 substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C₁₋₄alkyl, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), and -N(C₁₋₄alkyl)(C₁₋₄alkyl);

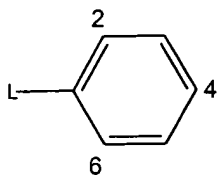
R_X and R_Y are the same or different and are independently selected from the group consisting of:

- B6
cont⁵
- hydrogen (with the proviso that R_X and R_Y are not both hydrogen),
 - $-(C=O)alkyl_A$, wherein $alkyl_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;
 - straight, branched, or cyclic alkyl groups, including cycloalkyl(alkyl), said straight, branched, or cyclic alkyl groups having from 1 to 8 carbon atoms, and containing zero, one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from hydroxy, halogen, amino, cyano, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, and $-NH(C_{1-4}alkyl)(C_{1-4}alkyl)$.

10

20. A compound or salt according to Claim 17, wherein

Ar is a phenyl group of the formula:



15

wherein L indicates a bond to the pyrimidine ring in Formula B

and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituents independently selected from:

- halogen, cyano, halo(C_{1-4} alkyl), halo(C_{1-4} alkoxy), hydroxy, amino, C_{1-6} alkyl, C_{1-6} alkoxy, (C_{1-4} alkoxy) C_{1-4} alkoxy, and mono- or di(C_{1-4} alkyl)amino,

20

ii) C_{1-6} alkyl and C_{1-6} alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C_{1-4} alkyl, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, and $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$;

25

R_X and R_Y are the same or different and are independently selected from the group consisting of:

- hydrogen (with the proviso that R_X and R_Y are not both hydrogen),

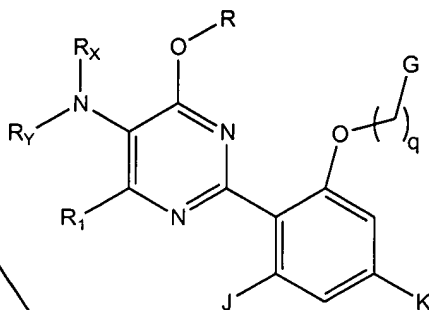
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cont

5

b) $(C=O)alkyl_A$, wherein $alkyl_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups, including cycloalkyl(alkyl) groups, said straight, branched, or cyclic alkyl groups have from 1 to 8 carbon atoms and may contain one or more double or triple bonds.

21. A compound or salt according to Claim 17, of the formula:



wherein:

10 q is an integer from 1 to 4;

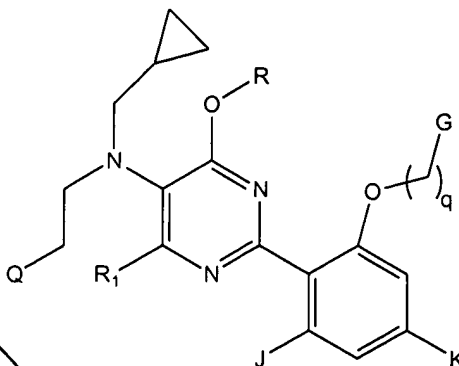
G is hydrogen, hydroxy, C_{1-6} alkoxy, $-NH(C_{1-6}alkyl)$, $-N(C_{1-6}alkyl)(C_{1-6}alkyl)$, or a 3- to 7-membered carbocyclic or heterocyclic group which is saturated, unsaturated, or aromatic, which is unsubstituted or substituted with one or more substituents independently selected from halogen, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, oxo, hydroxy, amino, C_{1-4} alkyl, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$, and $-S(O)_n(alkyl)$, wherein said 3- to 7-membered heterocyclic group contains one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen;

20 J and K are independently selected from halogen, cyano, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, hydroxy, amino, C_{1-6} alkyl, C_{1-4} alkyl, C_{1-4} alkoxy, $(C_{1-4}alkoxy)C_{1-4}alkoxy$, and mono- or di($C_{1-4}alkyl$)amino.

22. A compound or salt according to Claim 17, of the formula:

Sub
B7

B7
cont



wherein:

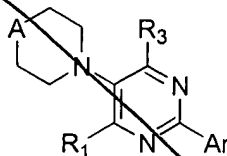
Q is hydrogen, C₃₋₇ cycloalkyl, pyrrolidinyl, piperidinyl, morpholino, or piperazinyl;
q is an integer from 1 to 4;

- 5 G is hydrogen, hydroxy, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), or a 3- to 7-membered carbocyclic or heterocyclic group, which is saturated, unsaturated, or aromatic, which is unsubstituted or substituted with one or more substituents independently selected from halogen, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, oxo, hydroxy, amino, C₁₋₄alkyl, -O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), and -S(O)_n(alkyl), wherein said 3- to 7-membered heterocyclic group contains one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen;

- 10 J and K are independently selected from halogen, cyano, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, hydroxy, amino, C₁₋₆ alkyl, C₁₋₄alkyl, C₁₋₄alkoxy, (C₁₋₄alkoxy) C₁₋₄alkoxy, and mono- or di(C₁₋₄alkyl)amino; and
- 15 R_X and R_Y are the same or different and are independently selected from hydrogen (with the proviso that R_X and R_Y are not both hydrogen) and straight, branched, or cyclic alkyl groups having from 1 to 6 carbon atoms, which alkyl groups may contain one or more double or triple bonds.

20

23. A compound or salt according to claim 3 of general the formula:



wherein:

Sub
E1

A is NH, N(C₁₋₆-alkyl), O, CH₂, or CH(C₁₋₆-alkyl).

24. A compound or salt according to Claim 1 wherein, in a standard in vitro CRF receptor binding assay the compound exhibits an IC₅₀ value less than or equal to 1 micromolar.

25. A compound or salt according to Claim 1 wherein, in a standard in vitro CRF receptor binding assay the compound exhibits an IC₅₀ value less than or equal to 100 nanomolar.

26. A compound or salt according to Claim 1 wherein, in a standard in vitro CRF receptor binding assay the compound exhibits an IC₅₀ value less than or equal to 10 nanomolar.

27. A method for treating an anxiety disorder, a stress-related disorder, or an eating disorder, comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or salt according to Claim 1.

28. A method for treating an depression or bipolar disorder, comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or salt according to Claim 1.

29. A method for treating anorexia nervosa, bulimia nervosa, or obesity, comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or salt according to Claim 1.

30. A compound or salt according to Claim 1, wherein in a standard in vitro Na channel functional assay the compound does not show any statistically significant activity at the $p < 0.05$ level of significance.

31. A method for localizing CRF receptors is tissue section samples comprising:
contacting with a sample of tissue a detectably-labeled compound or salt of Claim 1 under conditions that permit binding of the compound to CRF receptors within the sample of tissue;
washing the tissue sample to remove unbound compound; and
detecting remaining bound compound, wherein the detection of remaining bound compound is an indication of the presence of CRF receptors in the tissue sample.

32. A method of inhibiting the binding of CRF to the CRF1 Receptor which comprises:

contacting a solution comprising CRF and a compound or salt of Claim 1 with a cell expressing a CRF receptor, wherein the compound is present at a concentration sufficient to inhibit CRF binding to IMR32 cells *in vitro*.

33. The method of Claim 32 wherein the cell expressing a CRF receptor is a neuronal cell that is contacted *in vivo* in an animal, the solution is a body fluid.

34. The method of Claim 33 wherein the animal is a human, the cell is a brain cell, and the fluid is cerebrospinal fluid.

35. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound or salt of Claim 1.

36. A packaged pharmaceutical composition comprising a pharmaceutical composition of claim 35 in a container and instructions for using the composition to treat a patient suffering from an anxiety disorder, a stress-related disorder, or an eating disorder.

37. A packaged pharmaceutical composition comprising a

pharmaceutical composition of claim 35 in a container and instructions for using the composition to treat a patient suffering from depression or bipolar disorder.

38. A packaged pharmaceutical composition comprising a
5 pharmaceutical composition of claim 35 in a container and instructions for using the composition to treat a patient suffering from anorexia nervosa, bulimia nervosa, or obesity.

Sub
E1
39. A compound according to Claim 1, which is [2-(2,4-dimethoxyphenyl)-4-
10 methoxy-6-methylpyrimidin-5-yl]dipropylamine.

40. A compound according to Claim 1, which is [2-(2-chlorophenyl)-4-
methoxy-6-methylpyrimidin -5-yl]dipropylamine.

41. A compound according to Claim 1, which is [2-(2,4-dichlorophenyl)-4-
15 methoxy-6-methylpyrimidin -5-yl]dipropylamine.

42. A compound according to Claim 1, which is [2-(2-methoxy-4-
chlorophenyl)-4-methoxy-6-methylpyrimidin -5-yl]dipropylamine.

43. A compound according to Claim 1, which is [2-(2-methoxy-4-
20 isopropylphenyl)-4-methoxy-6-methylpyrimidin -5-yl]dipropylamine.

44. A compound according to Claim 1, which is [2-(2,4-dimethoxyphenyl)-4-
25 methoxy-6-methyl pyrimidin-5-yl] dipropylamine.

45. A compound according to Claim 1, which is [4-methoxy-2-(6-methoxy-
2,4-dimethylphenyl)-6-methylpyrimidin-5-yl]dipropylamine.

46. A compound according to Claim 1, which is [2-(2-methoxy-4,6-
30 dimethylphenyl)-4-methoxy-6-ethyl pyrimidin-5-yl] dipropylamine.

47. A compound according to Claim 1, which is [2-(2,4,6-trimethylphenyl)-4-methoxy-6-methyl pyrimidin-5-yl] dipropylamine.

5 48. A compound according to Claim 1, which is [2-(2,4,6-trimethylphenyl)-4-methoxy-6-ethyl pyrimidin-5-yl] dipropylamine.

49. A compound according to Claim 1, which is [2-(2-methoxy-4,6-dimethylphenyl)-4-ethoxy-6-methyl pyrimidin-5-yl] dipropylamine.

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50. A compound according to Claim 1, which is [2-(2-methoxy-4,6-dimethylphenyl)-4-(2-fluoroethoxy)-6-methyl pyrimidin-5-yl] dipropylamine.

15

51. A compound according to Claim 1, which is [2-(2-methoxy-4,6-dimethylphenyl)-4-isopropoxy-6-methyl pyrimidin-5-yl] dipropylamine.

52. A compound according to Claim 1, which is [2-(2-methoxy-4,6-dimethylphenyl)-4-methoxy-6-fluoromethyl pyrimidin-5-yl] dipropylamine.

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53. A compound according to Claim 1, which is [2-(2-methoxy-4,6-dimethylphenyl)-4-methoxy-6-difluoromethyl pyrimidin-5-yl] dipropylamine.

25

54. A compound according to Claim 1, which is 1-[5-(dipropylamino)-6-methoxy-2-(2-methoxy-4,6-dimethylphenyl)-pyrimidin-4-yl]-ethan-1-ol.

55. A compound according to Claim 1, which is 1-[5-(dipropylamino)-6-methoxy-2-(2-methoxy-4,6-dimethylphenyl)-pyrimidin-4-yl]-propan-2-ol.

30

56. A compound according to Claim 1, which is [4-(2-Cyclopropyl-2-fluoroethyl)-6-methoxy-2-(2-methoxy-4,6-dimethylphenyl)-pyrimidin-5-yl]-dipropyl-amine.

57. A compound according to Claim 1, which is [4-(2-Cyclopropyl-2-hydroxy-ethyl)-6-methoxy-2-(2-methoxy-4,6-dimethyl-phenyl)-pyrimidin-5-yl]-dipropylamine.

5 58. A compound according to Claim 1, which is 1-[5-Dipropylamino-6-methoxy-2-(2-methoxy-4,6-dimethyl-phenyl)-pyrimidin-4-ylmethyl]-cyclobutanol.

59. A compound according to Claim 1, which is (Cyclopropylmethyl)[4-methoxy-2-(6-methoxy-2,4-dimethylphenyl)-6-methylpyrimidin-5-yl]propylamine.

10

60. A compound according to Claim 1, which is Cyclopropylmethyl-[2-(2-ethoxy-4,6-dimethylphenyl)-4-methoxy-6-methyl pyrimidin-5-yl] propyl-amine.

15 61. A compound according to Claim 1, which is Cyclopropylmethyl[2-(2-propoxy-4,6-dimethylphenyl)-4-methoxy-6-methylpyrimidin-5-yl] dipropylamine.

62. A compound according to Claim 1, which is Cyclopropylmethyl[2-(2-isopropoxy-4,6-dimethylphenyl)-4-methoxy-6-methylpyrimidin-5-yl] dipropylamine.

20 63. A compound according to Claim 1, which is Cyclopropylmethyl[2-(2-ethoxymethoxy-4,6-dimethylphenyl)-4-methoxy-6-methylpyrimidin-5-yl] dipropylamine.

25 64. A compound according to Claim 1, which is [2-(dimethylamino)ethyl](cyclopropylmethyl)[6-methoxy-2-(6-methoxy-2,4-dimethylphenyl)-4-methylpyrimidin-5-yl]amine.

65. A compound according to Claim 1, which is Cyclopropylmethyl-[4-methoxy-2-(2-methoxy-4,6-dimethyl-phenyl)-6-methyl-pyrimidin-5-yl]-(2-pyrrolidin-1-yl-ethyl)-amine.

5 66. A compound according to Claim 1, which is Cyclopropylmethyl-[4-methoxy-2-(2-methoxy-4,6-dimethyl-phenyl)-6-methyl-pyrimidin-5-yl]-(2-morpholin-1-yl-ethyl)-amine.

67. Cyclopropylmethyl-(2-methoxy-ethyl)-[4-methoxy-2-(2-methoxy-4,6-
10 dimethyl-phenyl)-6-methyl-pyrimidin-5-yl]-amine.

68. A compound according to Claim 1, which is Cyclopropylmethyl-[4-methoxy-2-(2-methoxy-4,6-dimethyl-phenyl)-6-methyl-pyrimidin-5-yl]-(2-piperidin-1-yl-ethyl)-amine.

15